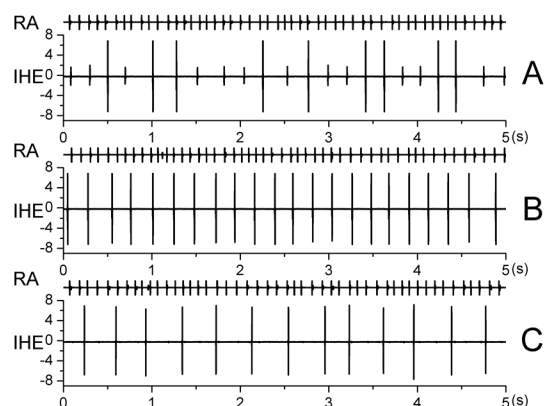


achieved only after collateral damage of the compact AVN. This study highlights the usefulness of HE alternans as a novel index to monitor AVN dual pathways and modification.



1034-208

Enalapril Can Prevent Perpetuation of Atrial Fibrillation Through Suppression of Interstitial Fibrosis and Connexin43 Expression Associated With Shortening of Excitable Gap in a Canine Rapid Atrial Pacing Model With Tachycardia-Mediated Cardiomyopathy

Masao Sakabe, Akira Fujiki, Kunihiro Nishida, Hidehiko Nagasawa, Koichi Mizumaki, Hiroshi Inoue, Toyama Medical and Pharmaceutical University, Toyama, Japan

Effects of enalapril on pacing-induced canine atrial fibrillation (AF) with rapid ventricular responses were investigated. Methods: Twenty-one beagles were pretreated with placebo (G-I, n=14) or enalapril 1mg/kg (G-II, n=7). All beagles were paced at 500bpm from the right atrial appendage for 4 weeks. Ventricular rate during pacing was similar (G-I 272.9±47.8bpm vs. G-II 279.5±33.4bpm; N.S.). Atrial effective refractory period (AERP), averaged P-wave width, inducibility of AF and duration of induced-AF were evaluated every week. Spectral analyses of fibrillation waves were performed to evaluate AF cycle length (FCL). The excitable gap (EG) was defined as FCL minus the shortest cycle length producing atrial capture. Left ventricular ejection fraction (LVEF) was measured with transthoracic echocardiography. After 4 weeks pacing, tissues were stained with Masson's trichrome and Connexin (Cx)43 and quantitative analysis was performed.

Results: The shortening of AERP after one week pacing did not differ (G-I 30.7±6.0%, G-II 25.6±17.5%). The inducibility of AF after 4 weeks pacing was similar, but the duration was significantly shorter in G-II (3.6±3.4sec) compared with G-I (58.0±60.0sec; p<0.05). The P-wave width was shorter in G-II (75.3±6.5ms) than G-I (85.5±13.0ms; p<0.05). FCL and EG were shorter in G-II (FCL 116.6±1.5ms, EG 14.1±10.3ms) than G-I (FCL 134.5±20.2ms; p<0.05, EG 34.7±14.1ms; p<0.05). LVEF was significantly decreased and it was similar in both groups (G-I 37.5±15.6%, G-II 37.4±1.2%). There were significant decrease in both interstitial fibrosis (IF) and Cx43 in G-II compared with G-I (IF: 2.2±2.3% vs. 9.2±9.1%; p<0.05, Cx43: 1.1±1.2% vs. 5.3±2.2%; p<0.05). Conclusions: Enalapril decreased prolongation of P-wave width and duration of AF owing to the suppression of IF and over-expression of Cx43 in this model. During induced AF enalapril decreased both FCL and EG without affecting AERP. These findings suggest enalapril can prevent perpetuation of AF with tachycardia-mediated cardiomyopathy through shortening of EG due to improvement of atrial conduction delay.

1034-209

Depression and Not Facilitation Governs the Atrioventricular Nodal Propagation: Insight From Dual Pathway Electrophysiology

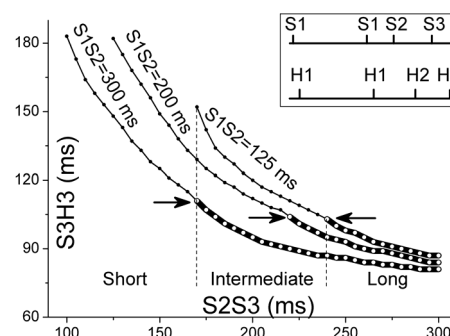
Yuhua Zhang, Todor N. Mazgalev, The Cleveland Clinic Foundation, Cleveland, OH

S1-S2-S3 atrial pacing protocols, with S1S2 interval interposed between basic S1 and test impulse S3 (figure, inset), are widely used to study functional properties of atrioventricular node (AVN). A controversial phenomenon, facilitation, has been observed with shortening of S1S2. We investigated the properties of fast and slow pathway (FP, SP) conduction, hypothesizing that facilitation reflects enhanced FP conduction when S1S2 is shortened.

Methods: AVN conduction curves were generated by programmed pacing in 7 rabbit hearts. For 3 S1S2 intervals (300, 150, 125 ms) conduction times S3H3 were plotted against prematurities S2S3. The segments of the curves corresponding to FP or SP conduction were defined by applying the sensitive index of His electrogram alternans (Circ 2003; 107:1059).

Results: Shortening of the interposed S1S2 shifted all conduction curves up and right (figure). AVN effective refractory period prolonged (102 ± 9 to 125 ± 14 to 156 ± 33 ms). Most importantly, the transition from FP (thick segments) to SP (thin segments) occurred at progressively longer test prematurity S2S3 (arrows, 175 ± 36 to 203 ± 42 to 244 ± 45 ms). Therefore, shortening of S1S2 did not facilitate any of the pathways. In contrast, there was either depression of FP (at Long S2S3), or block of FP and shift to SP (at Intermediate S2S3), or depression of SP (at Short S2S3).

Conclusion: Depression, not facilitation, is fundamental AVN property revealed by short interposed S1S2 intervals that produce inhibition of both the FP and SP.



1034-210

Mapping of Successful and Failed Atrial Defibrillation

Xiangsheng Zheng, Gregory P. Walcott, Raymond E. Ideker, University of Alabama at Birmingham, Birmingham, AL

We electrically mapped atrial defibrillation in 10 sheep with sustained atrial fibrillation induced electrically after pericardial infusion of methylcholine. Biphasic shocks (3-1 ms) with a peak voltage 5-10% lower than the atrial defibrillation threshold were delivered to right atrial and coronary sinus electrodes. In the first 8 sheep global atrial mapping was performed with 504 electrodes spaced 3-4 mm apart. Seventeen successful shocks were "type B" in which 1 or more rapid activations appeared after the shock. A long interval was present between the shock and earliest postshock activation for all episodes but was longer for type B (113±32 ms) then for failed (74±25 ms, p<0.05) episodes. In all type B and 17 of 24 failed episodes, activation spread way from the earliest activation in a focal pattern. In none of the type B and in 7 of the failed episodes, a region of approximately 10 to 40 electrodes with fragmented and double potentials exhibited earliest postshock activation. In those 17 failed episodes in which earliest activation was focal and in none of the type B episodes, regions of fragmented electrograms were observed during later activation cycles. Since the electrode spacing was too great in the global maps to map activation in the fragmented regions, in 2 additional sheep a 504 electrode plaque with 1.5 mm electrode spacing was placed on the right atrial appendage and all postshock episodes were analyzed. In 11 episodes in which earliest activation appeared inside the plaque, earliest activation was focal in 10. In the remaining 1 episode in which the earliest activated region exhibited fragmented electrograms, reentry could be identified. In those 10 failed episodes in which earliest activation was focal, regions of fragmented electrograms were observed during later activation cycles and reentry could be identified in 5. Thus, (1) earliest recorded postshock activation follows a relatively long interval after the shock and is longer for type B than failed episodes, (2) earliest activation following all type B and most failed episodes is focal, and (3) all failed but no type B episodes exhibit regions of fragmented electrograms which may represent reentry.

1034-211

Neutrophil Infiltration as an Inflammatory Mechanism Promoting Atrial Fibrosis in Atrial Fibrillation

David R. Van Wagoner, Rachel Jamison, Marie-Luise Brennan, Mina K. Chung, A. Marc Gillinov, Cleveland Clinic Foundation, Cleveland, OH

Background: We have postulated that inflammation contributes to structural remodeling that increases the persistence of atrial fibrillation (AF). Myocyte loss (apoptotic or necrotic) and replacement fibrosis are key elements of this process. Injured myocardium releases cytokines that recruit neutrophil and macrophage infiltration. Neutrophils help to remove necrotic or apoptotic myocytes. Myeloperoxidase (MPO) is an abundant neutrophil marker. In this study, we tested the hypothesis that atrial fibrosis is increased in the atria of AF patients, and that neutrophil infiltration was correlated with the extent of fibrosis.

Methods: Sections of left atrial appendage (LAA) were characterized from patients undergoing cardiac surgery (Maze surgery for AF, and/or mitral valve repair). Maze LAA (n=11) were from persistent AF patients. Control LAA (n=4) were from patients in normal sinus rhythm undergoing mitral valve repair. LAA were formalin-fixed, blocked and mounted for histologic analysis. Adjacent sections from each appendage were stained either with Masson's trichrome stain (to quantify fibrosis) or with an antibody to MPO. Fibrosis was quantified as the fraction of muscle bundles in cross-sections stained blue, using NIH Image analysis software.

Results: Interstitial fibrosis was significantly increased in AF tissues (47±6%) vs. controls (29±5%, p<0.001). In AF LAA, the correlation between extent of fibrosis and age was weak. Mean ages of the groups were similar (controls 66.3 years, AF 58 years). MPO staining was detectable in LAA from 4/11 AF patients. Inflammatory infiltration was typically most apparent at the border of normal myocardium and endocardial fibrosis, suggesting a causal relationship between the inflammatory process and development of fibrosis. Among the AF LAA, those with abundant MPO+ cells had significantly higher interstitial fibrosis (51±1%) relative to those without MPO staining (44±2%, p=0.037).

Conclusions: Low-level inflammation accompanying persistent AF likely reflects ongoing apoptosis and replacement fibrosis. MPO staining suggests that neutrophil activation has a prominent role in the structural remodeling that promotes AF persistence.